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RESEARCH ARTICLE

Risk Factors of Gastric Ulcers in Dogs

Marcin Jankowski[1*], Jolanta Spużak[1], Krzysztof Kubiak[1], Kamila Glińska-Suchocka[1], Monika Biernat[2] and Zdzisław Kiełbowicz[3]

[1]Department of Internal Diseases with Clinic of Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wroclaw University of Environmental and Life Sciences, Pl. Grunwaldzki 47, 50-366 Wroclaw, Poland; [2]Department of Microbiology, Faculty of Medicine, Wroclaw Medical University, ul. T. Chałubińskiego 4, 50-368 Wroclaw, Poland; [3]Department of Surgery, Faculty of Veterinary Medicine, Wroclaw University of Environmental and Life Sciences, Pl. Grunwaldzki 51, 50-366 Wroclaw, Poland
*Corresponding author: jank1973@tlen.pl

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ABSTRACT

The aim of the study was to identify the risk factors causing gastric ulcer formation in dogs and determining the prevalence of their occurrence. The study group consisted of 49 dogs of different breeds and genders, between 1-16 years of age. All the dogs were found to have gastric ulcers during an endoscopic examination. The differentiation of peptic ulcers from gastric neoplastic ulcers was based on a histopathological examination, whereas *Helicobacter* sp. was detected through PCR-assays. Peptic ulcers were diagnosed in 40 dogs and gastric neoplasia was identified in 9 dogs. 46 dogs tested positive for *Helicobacter* sp. The study confirmed a multifactorial cause of gastric ulcers, where the greatest risk factor of peptic ulcers in dogs was the usage of non-steroidal anti-inflammatory drugs, whereas adenocarcinoma was the greatest risk factor of gastric ulcers of neoplastic origin.

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INTRODUCTION

Gastric ulcers are one of the most frequently recognized disorders affecting the anterior segment of the gastrointestinal tract in dogs. They can develop independently in the stomach, as a complication of systemic diseases, or they can form in response to the use of certain drugs. Gastric ulcers are formed when the protective barrier of the so called gastric mucosal cytoprotective barrier is broken by the so called "aggressive factors" (Kubiak *et al.,* 2004a). These aggressive factors include hydrochloric acid, pepsin, trypsin, stimulants of hydrochloric acid secretion, oxygen free radicals, drugs (NSAIDs), platelet activating factors and bile acids (Parrah *et al.,* 2013). In humans, a *Helicobacter pylori* infection is also considered an aggressive factor in ulcer disease (Kate *et al.,* 2013). On the other hand, gastric mucosal protective factors include gastric mucus, tight junctions between epithelial cells, rapid epithelial regeneration, bicarbonate secretion, production of prostaglandins, presence of gastrointestinal and pancreatic peptides, the production of the epithelial growth factor and an adequate gastric mucosal blood flow (Houszka, 1998). The aim of the study was to identify the risk factors causing gastric ulcer formation in dogs and determining the prevalence of their occurrence.

MATERIALS AND METHODS

The study was conducted on 49 dogs of different breeds and sex, 1-16 years of age, in whom a gastroscopy showed gastric ulcers. Prior to the gastroscopy, all the dogs were subjected to a clinical examination, a hematological and biochemical blood test and an ultrasonography of the abdominal cavity. The animals fasted for at least 24 hours for solids and 6 hours for water prior to the endoscopic examination. It was carried out under general anesthesia using propofol, and the premedication was performed using xylazine and atropine. The gastroscopy was performed using an Olympus GIF XQ-20 flexible endoscope.

A diagnosis of ulcer's risk factors in the study group was based on: anamnesis, clinical examination, blood tests, ultrasound examination of the abdomen, gastroscopy and histopathologic assessment of samples.

The gastric mucosa samples were collected from the ulcer area using Olympus FB-45-1 "alligator jaw" biopsy forceps for a histopathological and PCR examination, the

latter of which was carried out to determine the presence of the *Helicobacter* species in the specimens. For the histopathological examination, the bioptates were fixed in a 4-10% buffer formalin solution. The tissue slices were stained with hematoxylin and eosin. The inflammatory lesions of the gastric mucosa were examined according to the Sydney classification. The bioptates for the PCR examination were frozen and sent to the laboratory for further testing.

RESULTS

Characteristics of the examined group Gastric ulcers were diagnosed in 22 breeds: terriers - 8 cases (American Staffordshire Terrier - 2 cases, West Highland White Terrier - 2 cases, Scottish Terrier - 1 case, Staffordshire Bull Terrier - 1 case, Welsh Terrier - 1 case, Wire Fox Terrier - 1 case), German Shepherd Dog - 7 cases, Chow Chow - 3 cases, Doberman - 3 cases, Boxer - 2 cases, Cocker Spaniel - 2 cases, Labrador Retriever - 2 cases, Shar pei - 2 cases, Beagle - 1 case, Bobtail - 1 case, Border Collie - 1 case, Dachshund - 1 case, Golden Retriever - 1 case, Munsterlander - 1 case, Pinscher - 1 case, Standard Schnauzer - 1 case, Weimaraner - 1 case and 11 cases of mixed breed dogs. Gastric ulcers were found to occur most frequently in mixed breed dogs. Gastric ulcers occurred in males - 33 (67.3%) cases - more often than in females - 16 (32.7%) cases. Dogs with gastric ulcers were on average 7.5 (±4.2) years old. Nineteen dogs (38.8%) had an age between 1 and 5 years, 15 (30.6%) dogs were between 6 and 10 years old and 15 (30.6%) were at least 10 years old.

Of the 49 dogs diagnosed with gastric ulcers, 40 (81.6%) were diagnosed with peptic ulcers and 9 (18.4%) were diagnosed with gastric neoplasia. The causes of peptic ulcers were determined in 36 (90%) cases. These included: chronic renal failure in two cases, duodenogastric reflux in seven cases, oral administration of non-steroidal anti-inflammatory drugs in 11 cases (Fig. 1.), hypertrophic pyloric stenosis in three cases, stomach foreign bodies in six cases (Fig. 2.), liver failure in three cases, Cushing's syndrome in one case, ingesting a caustic agent in one case and administration of glucocorticoids in two cases. In four cases (10%), the etiological factor of gastric ulcers could not be determined. In the group with non-steroidal anti-inflammatory drugs as causative agents (n=11) nine dogs (81.8%) had received NSAIDs of the first generation NSAIDs - ibuprofen, ketoprofen and piroxicam, and two dogs (18.2%) developed gastric ulcers after receiving a second generation NSAID - carprofen. The histopathological examination revealed that the most common type of stomach neoplasia was adenocarcinoma (8 cases - 88.8%) (Fig. 3), whereas lymphoma was diagnosed in one dog (11.2%).

First generation NSAIDs were administered *per os* to the patients without medical prescription for 2 - 5 days single time a day in following dosages: ibuprofen - 200 mg/dog, ketoprofen - 50 mg/dog and piroxicam - 20 mg/dog. Whereas carprofen was administered to the patients following veterinary surgeons advice: in dosage 4 mg/kg, *per os*, SID for two months. Dogs were gastric ulcers were caused by corticosteroids administration were treated with prednisone 0.5 mg/kg *per os*, BID for 2 months in one case and for 2.5 months in second case.

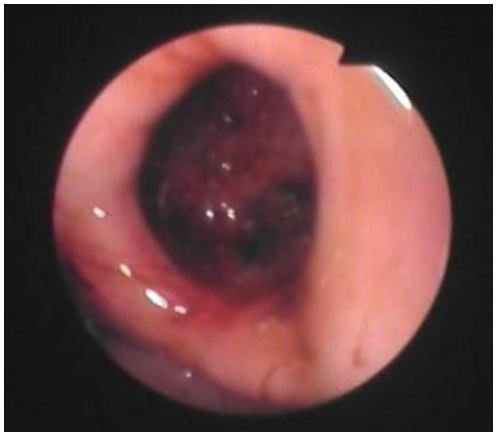

Fig. 1: A pyloric peptic ulcer in a dog that received non-steroidal anti-inflammatory drugs

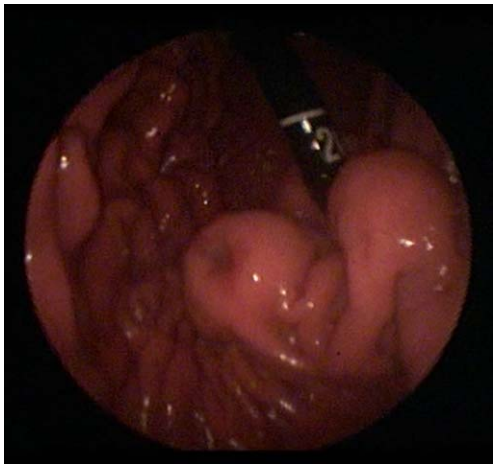

Fig. 2: A small ulcer in the cardia part of the stomach caused by a foreign body

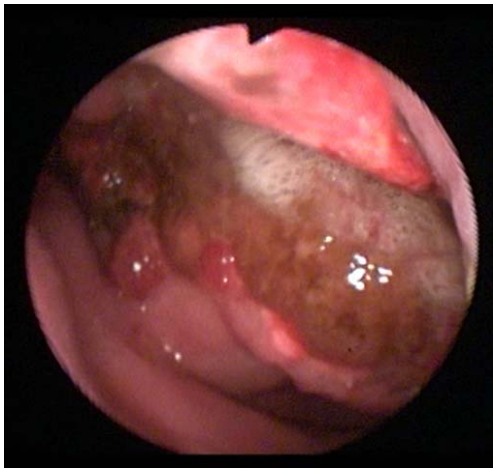

Fig. 3: Non-peptic ulcer associated with gastric adenocarcinoma

On the basis of endoscopic examination, large gastric ulcers with marginal folds and deep ulcer niches were seen in 9 dogs (18.4%), while 31 dogs (63.2%) had small ulcers with poorly demarcated marginal folds and shallow ulcer niches. Both types of ulcers were recognized in nine dogs (18.4%).

The ulcers were located in the corpus, pylorus and cardia of the stomach. There was an almost equal distribution of ulcers in the corpus (29 cases - 59.2%) and pylorus (30 cases - 76.9%) of the stomach. Fewer ulcers were seen in the cardia of the stomach (9 cases - 18.4%).

Inflammatory lesions of the mucosa in all dogs accompanied gastric ulcers. Based on the histological division of the Sydney system, severe chronic gastritis was present in 11 cases (22.6%), moderate chronic gastritis in 14 cases (28.5%) and mild chronic gastritis in 24 cases (48.9%).

Based on PCR assays, the presence of *Helicobacter* bacteria was confirmed in 46 dogs (93.9%) with gastric ulcers. Twenty nine dogs (63%) were infected with one species of *Helicobacter* (*H.*), of which *H. heilmannii* was detected in 17 dogs, *H. felis* in 7 dogs, *H. pylori* in 3 dogs and *H. salomonis* in 2 dogs. Sixteen dogs were infected with two species of *Helicobacter* in the following configurations: *H. heilmannii* + *H. felis* - 15 cases and *H. heilmannii* + *H. salomonis* – one case. One dog was found to be infected with three *Helicobacter* species - *H. heilmannii* + *H. felis* + *H. salomonis*. Only three dogs (6.1%) were free from a *Helicobacter* sp. infection. The most common species identified in dogs with gastric ulcers was *H. heilmannii* - 34 cases. *H. felis* was detected in 23 dogs, *H. salomonis* was found in 4 dogs and *H. pylori* was identified in 3 dogs.

DISCUSSION

Gastric ulcers have been described in many species of domestic animals. They have been found to occur most frequently in horses, dogs and cats; much less frequently in pigs and least frequently as abomasal ulcers in cattle (Kubiak *et al.,* 2004a; Parrah *et al.,* 2013). Hitherto, no sex, age or breed predispositions to gastric ulcers have been found (Stanton and Bright, 1989). Our own observations confirm this. However, we have found that gastric ulcers occurred more frequently in males (67.3%) and mixed breed dogs (22.5%). This could have been caused by the fact that more endoscopic examinations of the anterior segment of the gastrointestinal tract were carried out in males than females in the endoscopic laboratory. This has been confirmed in a statistical analysis of patients between 2011 and 2013, where the male-to-female patient ratio was 64:34 (65.3%: 34.7%), 68:41 (62.4%: 37.6%) and 55:41 (56.1%: 43.9%) respectively in the three consecutive years. The average of male dogs in the three year period was 62.1 ± 6.7 (61.3±4.7%). Similarly, mixed breed dogs constituted 17.3%, 14.3% and 24.5% (average - 18.8% ± 5.1%) of the population respectively in the three years.

Risk factors occurrence may lead to non-cancerous stomach ulcers, named peptic ulcers, and neoplastic ulcers. The former include: mechanical damage, chemical agents, systemic diseases and stress (Parrah *et al.,* 2013). Risk factors for neoplastic ulcers, on the other hand, are stomach cancer such as adenocarcinoma and lymphoma. In dogs, peptic ulcers are the most frequently diagnosed ulcers (Kubiak *et al.,* 2004a). Our own study, where peptic ulcers comprised 81% of gastric ulcers in dogs, confirms this finding.

Dogs treated with NSAIDs for chronic pain and inflammatory musculoskeletal disease, as well as those treated with these drugs by their owners who do not consult such treatment with a veterinary surgeon, are particularly exposed to their adverse effects on the gastrointestinal tract (Ramprabhu *et al.*, 2001). Despite a fairly wide use of NSAIDs in veterinary medicine, there is no data regarding the frequency of their administration or gastrointestinal tract complications associated with their use. In humans, complications connected with using NSAIDs have been of major concern for many years due to their availability and widespread frequency of application. It is currently believed that gastric ulcers develop in 15-40% of patients and duodenal ulcers develop in 20% of patients who are on long-term NSAIDs treatment (Wallace, 1996; Sostres *et al.*, 2013). Our study has shown that an administration of NSAIDs in dogs was the most common cause of gastric ulcers (accounting for 22.4% of all ulcers) and led to the formation of large and giant ulcers. A study by Stanton and Bright (1989) confirms this. Non-steroidal anti-inflammatory drugs act by inhibiting the activity of cyclooxygenase - an enzyme involved in arachidonic acid metabolism. To date, three cyclooxygenase isoforms have been identified - COX-1 (the end products are involved in physiological processes), COX-2 (the end products are involved in pathological processes) and COX-3 (the role of this isoform in the inflammatory process remains unclear). First generation NSAIDs inhibit COX-1 and COX-2. The synthesis of gastroprotective agents such as prostaglandins and prostacyclin is impaired through the inhibition of COX-1. These gastroprotective agents are responsible for the inhibition of leukotriene function (leukotrienes secrete hydrochloric acid and pepsinogen), protection of gastric mucosal microcirculation, stimulation of the synthesis and secretion of surface mucus, an increase in bicarbonate secretion and an acceleration of gastrointenstinal epithelium regeneration. Second generation NSAIDs, which selectively inhibit COX-2, seem to be safer (Szweda *et al.,* 2013). However, an inhibition of COX-2 leads to an activation of the lipoxygease pathway, whose end products are leukotrienes that damage gastrointestinal mucosa (Wooten *et al.*, 2010). NSAIDs can also cause toxic local damage to the gastric mucosa. The direct action of NSAIDs on the gastric mucosa is manifested by an impairment of mitochondrial function, which leads to an ATP deficiency, thus rendering epithelial cells susceptible to oxidative stress (Wallace, 1996).

It is currently believed that corticoids are much less likely to cause gastrointestinal complications, such as gastric ulcers, than non-steroidal anti-inflammatory drugs (Neiger *et al.,* 2000; Hsiang *et al.*, 2010; Zaki and Mohamed, 2012). Our study, where the use of these drugs led to gastric ulcers in 4.1% of dogs, confirms this. In veterinary medicine, animals with musculoskeletal system disorders and those disorders that require immunosuppressive treatment are exposed to adverse effects of glucocorticoids. There are several mechanisms, through which glucocorticoids act adversely on the gastric mucosa. These include: an increased secretion of gastrin, parietal cell hyperplasia, a reduction in the stomach's mucus production as well as an inhibition in arachidonic acid metabolism and prostaglandin synthesis (Hsiang *et al.*, 2010). The studies by Neiger *et al.* (2000) and Dowdle *et al.* (2003) confirm an adverse effect of glucocorticoids on the stomach. They demonstrated that 76% and over 76%

(respectively) of dogs with intervertebral disc disease, which received dexamethasone and prednisolone developed gastric mucosal inflammation and gastric ulcers. At the same time, in dogs with concurrent degenerative disc lesions could have been additional factors (e.g. sympathetic–parasympathetic imbalance, pain and surgical stress, hypotension) leading to such changes (Neiger *et al.,* 2000). On the other hand, in a study conducted on rats, Zaki and Mohamed (2012) showed that glucocorticoids did not have any adverse effects on the gastric mucosa when used in therapeutic doses. They concluded that glucocorticoids have a gastropathic effect when used in conjunction with non-steroidal anti-inflammatory drugs. This combination inhibits the regeneration of the gastric mucosa by preventing epithelial cell proliferation, angiogenesis and prostaglandin synthesis.

Gastric ulcers can be a result of mechanical damage of the gastric mucosa. Such damage is most often produced by those foreign bodies that are subject to retention in the stomach for lengthened periods of time and those with sharp ends. They act adversely through irritation and/or disruption of the continuity of the gastric mucosa. Due to the constant irritation of the gastric mucosa, they also stimulate gastrin secretion, which leads to an increase in the secretion of hydrochloric acid by parietal cells (Parrah *et al.,* 2013). Foreign bodies most often lead to the formation of small ulcers affecting the pyloric area. In the studied group, foreign bodies caused small ulcers in 12.2% of dogs. A similar mechanism of ulcer formation occurs in the case of hypertrophic pyloric stenosis, where the passage of gastric contents is disturbed and it undergoes retention in the stomach. This was a cause of ulcers in 6.1% of dogs in this study.

A duodenogastric reflux is yet another cause of adverse effects on the gastric mucosa. It can lead to a variety of lesions, including inflammatory changes, ulcer formation and intestinal metaplasia, which is considered an intermediate step in the development of gastric neoplasia. It can occur sporadically in dogs and is then considered a physiological phenomenon (Romański, 2010). It is only when there is an increase in the regurgitation of duodenal contents into the stomach that pathological lesions in the gastric mucosa occur, as a result of the disruption of the stomach protective barrier. The most common causes of a duodenogastric reflux are: surgical procedures carried out on the stomach and bile ducts and motility disorders of the stomach and duodenum (Romański, 2010). It is worth stressing that a duodenogastric reflux predisposes to a gastroesophageal reflux. The gastropathic substances acting during a duodenogastric reflux include duodenal contents containing bile, pancreatic and intestinal enzymes (Rychlik *et al.,* 2003; Vere *et al.,* 2005). Duodenal contents acts adversely on the gastric mucosa through: impairing mucus production, damaging epithelial cell membranes of the gastric mucosa through dissolving phospholipids and cholesterol and changing ion permeability (increased Na^+ diffusion into the gastric lumen, increased H^+ back diffusion through the mucosa). The degree of gastric mucosal damage depends on the pH in the stomach. The lower it is, the greater the damage to the mucosa (Rychlik *et al.,* 2003; Romański, 2010). In our study, a duodenogastric reflux was the cause of small, numerous ulcers in 14.3% of cases.

Liver disease, kidney disease, hyperadrenocorticism and shock are systemic diseases that can cause gastric ulcers (Parrah *et al.,* 2013). There are a number of mechanisms that lead to gastric mucosa damage in liver and kidney failure. One of these is the triggering of an increased secretion of gastric hydrochloric acid associated with a disturbed feedback between hydrochloric acid, gastrin and histamine, caused by a reduced removal of the latter two substances from the circulation. Another mechanism is vascular injury of the gastric mucosa, leading to ischemia and epithelial cell damage due to hypoxia. In renal failure, ammonia produced by bacteria in the course of urea degradation also leads to the damage of the gastric mucosa (Duerr *et al.,* 2004; Wasińska-Krawczyk *et al.,* 2006). The occurrence of gastric ulcers in the course of renal failure in dogs is rare which has been confirmed by Peters *et al.* (2005). In a group of 28 dogs that died or were euthanized because of renal insufficiency gastric ulcers were diagnosed only in one case, which was not confirmed by histopathologic examination. In Authors research renal insufficiency was a cause of gastric ulcers only in 4.1% of dogs. Furthermore it was established that a reason of gastric ulcers in 6.1% of dogs was liver insufficiency. Stanton and Bright (1989) reported different results, and found liver failure to be the second most common factor predisposing dogs to gastric ulcers. However, since the time that studies were conducted, there have new developments in the diagnostics and therapeutics of liver disease, which could reduce the occurrence of ulcers.

The most important risk factor of non-peptic ulcers in dogs is gastric neoplasms. They occur rarely and comprise less than 1% of all neoplasms in dogs. However, 60-70% of them are malignant, with adenocarcinoma occurring most commonly (Babo *et al.,* 2012; Seim-Wikse *et al.,* 2013). Neoplasms can disturb circulation in the blood vessels of the gastric mucosa leading to hypoxia, which often results in the formation of ulcers. Neoplastic ulcers are usually large, have an irregular fold and are prominent (Kubiak *et al.,* 2004b). This was confirmed in this study, where gastric neoplasia occurred in 18.4% of all cases. Neoplastic ulcers were giant and were localized on the lesser curvature of the stomach and in the pyloric area.

In humans, an infection with *H. pylori* is considered a major cause of gastritis, gastric ulcers and gastric neoplasia such as adenocarcinoma and lymphoma (Joosten *et al.,* 2013). The incidence of *H. pylori* infection in humans is high (Haesebrouck *et al.,* 2009). An infection with *Helicobacter* is equally prevalent in dogs, where *Helicobacter* was detected in 67-100% of healthy animals, in 100% of laboratory beagle dogs and shelter dogs, and in 61-95% of chronically vomiting dogs (Neiger and Simpson, 2000). Our own study confirmed a high prevalence of *Helicobacter* sp. in dogs, as it was detected in 90% of the study group. The following species of Helicobacter can be detected in the stomach of dogs: *H. heilmannii*, *H. felis*, *H. salomonis*, *H. bizzozeronii*, *H. pylori*, *H. rappini*, *H. bilis* and *H. cynogastricus*. Of these, *H. heilmannii* and *H. felis* are the most commonly detected species (Haesebrouck *et al.,* 2009). This is consistent with our study in which *H. heilmannii* and *H. felis* constituted 82.6% and 50% of cases respectively. The adverse effects of *Helicobacter* sp. have been determined based on *H. pylori*. The pathogenic mechanisms of *H. pylori* include the production of urease,

which breaks down urea into ammonia and bicarbonate ions (this factor enables the colonization of the gastric mucosa because it protects bacteria from gastric juice), adhesins (they enable bacteria to remain in the mucus layer and adhere to epithelial cells), the production of Vac A and Cag A cytotoxins (which enable vacuolation and induction of apoptosis of epithelial cells) and the activation of proinflammatory cytokines - interleukins IL-1b, IL-6, IL-8 and TNF-α. These cytokines cause disturbance of mucosal microcirculation, leading to the formation of hypoxic areas susceptible to hydrochloric acid, a decrease in the secretion of somatostatin, and a stimulation of gastrin secretion, which in turn stimulates gastric hydrochloric acid secretion (Kate *et al.,* 2013). The importance of an infection with *Helicobacter* sp. in the development of pathological gastric lesions is controversial. Although it has been found that a natural and experimental infection with *Helicobacter* sp. may lead to mild gastritis with a lymphocyte and plasma cell infiltration, it is still unclear why some animals develop an inflammatory reaction and others do not (Haesebrouck *et al.,* 2009; Joosten *et al.,* 2013). The authors of the present study found that a *Helicobacter* infection very often accompanied gastric ulcers although it was not possible to demonstrate a direct relationship between such an infection and ulcer formation. It is difficult to prove a link between a *Helicobacter* sp. infection and gastric ulcers because *Helicobacter* bacteria are highly prevalent in dogs, and it is thus difficult to find a control group. Secondly, there is a large diversity of the bacterial species that can colonize the stomach. Thirdly, strains within one species have different virulence.

Conclusion: No predisposition of dogs to gastric ulcers linked with breed, age or sex was found. Nevertheless, a multifactorial cause of gastric ulcers was confirmed, wherein the most common risk factor of gastric ulcers was the use of non-steroidal anti-inflammatory drugs. Adenocarcinoma was the greatest risk factor of gastric ulcers of neoplastic origin. The importance of a *Helicobacter* sp. infection in the development of gastric ulcers is still controversial and requires further research.

REFERENCES

Babo von V, N Eberle, R Mischke, A Meyer-Lindenberg, M Hewicker-Trautwein, I Nolte and D Betz, 2012. Canine non-hematopoietic gastric neoplasia. Epidemiologic and diagnostic characteristics in 38 dogs with post-surgical outcome of five cases. Tierärztl Prax, 40: 243-249.

Dowdle SM, KE Joubert, NE Lambrechts, RG Lobetti and AD Pardini, 2003. The prevalence of subclinical gastroduodenal ulceration in Dachshunds with intervertebral disc prolapse. J S Afr Vet Assoc, 74: 77-81.

Duerr FM, AP Carr, TN Bebchuk and NC Pople, 2004. Challenging diagnosis - icterus associated with a single perforating duodenal ulcer after long-term nonsteroidal anti-inflammatory drug administration in a dog. Can Vet J, 45: 507-510.

Haesebrouck F, F Pasmans, B Flahou, K Chiers, M Baele, T Meyns, A Decostere and R Ducatelle, 2009. Gastric Helicobacters in domestic animals and nonhuman primates and their significance for human health. Clin Microbiol Rev, 22: 202-223.

Houszka M, 1998. Gastropatyczne działanie niesterydowych leków przeciwzapalnych. Med Weter, 54: 594-597.

Hsiang KW, YY Ng, ChL Lu, TS Chen, HY Lin, JCh Luo, JM Wu, HCh Lin, FY Chang and SD Lee, 2010. Corticosteroids therapy and peptic ulcer disease in nephrotic syndrome patients. Br J Clin Pharmacol, 70: 756-761.

Joosten M, C Blaecher, B Flahou, R Ducatelle, F Haesebrouck and A Smet, 2013. Diversity in bacterium-host interactions within the species *Helicobacter heilmannii* sensu stricto. Vet Res, 44: 1-10.

Kate V, N Ananthakrishnan and FI Tovey, 2013. Is *Helicobacter pylori* infection the primary cause of duodenal ulceration or a secondary factor? A review of the evidence. Gastroenterol Res Pract, 2013: 1-8.

Kubiak K, J Nicpoń, M Jankowski, J Nicpoń and J Spużak, 2004a. Wrzody żołądka u psów. Med Weter, 60: 708-710.

Kubiak K, M Jankowski, J Nicpoń and J Spużak, 2004b. Gastroskopia w rozpoznawaniu nowotworów żołądka u psów. Med Weter, 60: 836-838.

Neiger R and KW Simpson, 2000. *Helicobacter* infection in dogs and cats: facts and fiction. J Vet Intern Med, 14: 125-133.

Neiger R, F Gaschen and A Jaggy, 2000. Gastric mucosal lesions in dogs with acute intervertebral disc disease: characterization and effects of omeprasole or misoprostol. J Vet Intern Med, 14: 33-36.

Parrah JD, BA Moulvi, MA Gazi, DA Makhdoomi, H Athar, S Dar and AQ Mir, 2013. Gastric ulceration in dog: A review. Vet World, 6: 449-454.

Peters RM, RE Goldstein, HN Erb and BL Njaa, 2005. Histopathologic features of canine uremic gastropathy: A retrospective study. J Vet Intern Med, 19: 315-320.

Ramprabhu RA, S Prathaban, AP Nambi, B Nagarajan and P Dhanapalan, 2001. Endoscopic evaluation of gastric mucosa after oral administration of ibuprofen in dogs. Vet Arhiv, 71: 47-51.

Romański K, 2010. Zarzucanie treści do żołądka i przełyku: problem u człowieka i zwierząt. Życie Wet, 85: 143-148.

Rychlik A, R Nieradka, M Kander and M Nowicki, 2003. Refluks dwunastniczo-żołądkowy u psów. Med Weter, 59: 973-975.

Seim-Wikse T, E Jörundsson, A Nódtvedt, T Grotmol, ChR Bjomvad, AT Kristensen and E Skancke, 2013. Breed predisposition to canine gastric carcinoma - a study based on the Norwegian canine cancer register. Acta Vet Scand, 55: 1-6.

Sostres C, CJ Gargallo and A Lanas, 2013. Nonsteroidal anti-inflammatory drug and upper and lower gastrointestinal mucosal damage. Arthritis Res Ther, 15 Suppl 3: 1-8.

Stanton ME and RM Bright, 1989. Gastroduodenal ulceration in dog - retrospective study of 43 cases and literature review. J Vet Intern Med, 3: 238-244.

Szweda M, J Szarek, K Dublan, M Gesek and T Mecik-Kronenberg, 2013. Effect of selected non-steroidal anti-inflammatory drugs on the pathomorphology of the mucous membrane of the canine colon. Vet Med, 58: 430-436.

Vere CC, S Cazacu, V Comănescu, L Mogoantă, I Rogoveanu and T Ciurea, 2005. Endoscopical and histological features in bile reflux gastritis. Rom J Morphol Embryol, 46: 269-274.

Wallace JL, 1996. NSAID gastroenteropathy: past, present and future. Can J Gastroenterol, 10: 451-459.

Wasińska-Krawczyk A, B Fiderkiewicz and A Rydzewski, 2006. Zaburzenia gastroenterologiczne u pacjentów z przewlekłą chorobą nerek. Prz Gastroenterol, 1: 192-196.

Wooten JG, BD Lascelles and VL Cook, 2010. Evaluation of relationship between lesions in the gastroduodenal region and cyclooxygenase expression in clinically normal dogs. Am J Vet Res, 71: 630-635.

Zaki SM and EA Mohamed, 2012. Effect of glucocorticoids on indomethacin-induced gastric ulcer in the adult male albino rat - histological, morphometric and electron microscopy study. Arch Med Sci, 8: 1-8.